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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,035	10/31/2003	John Francis Bateman	A36056-PCT-USA-A	3842

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,035	BATEMAN ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006 and 02 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,12,43 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,12,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/06& 10/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 10/2/06 and 11/2/06, is acknowledged.

2. Claims 4-5, 12, 43-44 are pending and under examination as it reads on an isolated polypeptide, derivative or homolog thereof of WARP and a polypeptide of human WARP of SEQ ID NO: 6 encoded by SEQ ID NO:5 and the VA domain of SEQ ID NO:2 encoded by SEQ ID NO: 1 as the species.

3. In view of the amendment filed on 10/2/06 and 11/2/06, only the following rejections are remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 4-5, 12 and 43-44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to used the claimed invention for the same reasons set forth in the previous Office Action mailed 3/31/06.

In order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to identify the function of the invention. Until the time when function of the invention is found, then one skill in the art can use the claimed WARP polypeptides of the invention. While the specification asserts specific utilities for the claimed WARP polypeptides as a molecular marker of the integrity of the extracellular matrix in an animal including a human subject, however, the specification says nothing on how the skilled in the art were going to measure WARP for ECM integrity. Is WARP elevated, decreased? The killed artisan would not know how to use WARP polypeptides to predict integrity?

Further, given the breadth encompassed by the instant claims, Applicant has not provided the skilled artisan with sufficient guidance as to the identity of all residues to be changed, to be left unchanged, to be deleted, or to have additional (unidentified) sequences inserted between. Without clear direction and guidance as to the nature of the changes made to a reference WARP sequence, the skilled artisan would be faced with undue experimentation to produce the immense number of "derivative" and "homolog" that *in situ* forms part of the extracellular matrix encompassed by the instant claims and determine if there were any operative embodiment that would result in the recited functional activity. Thus the specification does not appear to provide the skilled artisan with sufficient guidance to make and use such "derivative" and "homolog", commensurate in scope with the claimed invention.

The fact that two nucleic acid sequences will hybridize under stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "a nucleic acid that hybridizing to full-length" as were noted with respect to "derivative or homolog" language. A great deal of sequence variability *with respect to the full-length nucleic acid* is possible. As is evidence by claim 6, wherein the polypeptide is SEQ ID NO: 6. It is noted that claim 6 is not encoded by SEQ ID NO:5. However, a nucleic acid encoding SEQ ID NO: 6 would hybridize to the full-length of SEQ ID NO:5 under stringent conditions.

Also, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Accordingly, it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant's arguments, filed 10/2/06 and 11/2/06, have been fully considered, but have not been found convincing.

Applicant submits that the pending claims meet both the written description and enablement requirements. Applicant further submits that it is well within the skill of one in the art to identify a nucleic acid or polypeptide sequence having the similarity as claimed in the instant claims. Applicant points to the EST database at the NCBI was searched using the N8 VA-domain protein sequence as a query to identify EST sequences that contain the VA-domain (¶10). Also, a series of overlapping EST clones with homology to N8 represented a novel VA protein, therein entitled WARP (¶131&153).

However, a person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for integrity of ECM. Without detailed direction as to which amino acid sequences are essential to the function of the WARP polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the ability as a marker for ECM integrity of the encoded polypeptide of SEQ ID NO:6.

Applicant argues that the claims are not directed to the use of a polypeptide of the invention as a marker for ECM integrity. Rather, the claims are directed to an isolated polypeptide which, "*in situ* forms part of the ECM in an animal". Applicant points to the specification to provide support for the polypeptide as part of the ECM, as shown by the expression of WARP in cartilage (¶ 50 and 51), as well as by the teaching of Allen et al.

The recitation "*in situ* forms part of the ECM in an animal" is not seen as providing a requisite functional activity for the claimed amino acid encoded by the nucleic acid, in the absence of *a*

testable function, because there are still numerous functional activities encompassed besides it present in ECM.

Applicant further argues that a showing of the correlation of WARP with ECM integrity is not necessary. Applicant contends that one of skill in the art would know that WARP is normally associated with the ECM generally and interacts with perlecan. Applicant further submits that one skilled in the art would know that perturbations in WARP function or level would have an effect on the ECM. Applicant directs the Examiner's attention to Arikawa-Hirasawa (I) et al and Arikawa-Hirasawa (II) et al for support that WARP interacts with perlecan.

However, both references fail to provide evidence that supports Applicant's original assertion. It is noted that the specification fails to assert that WARP interacts with perlecan, Applicants cannot add to their original assertion to satisfy the enablement requirement on how to make and how to use. Furthermore, neither Arikawa-Hirasawa (I) or Arikawa-Hirasawa (II) teaches that WARP interacts with perlecan, or contemplated perturbations in WARP function or level would have an effect on the ECM. It seems that Applicants based their assumption on Allen's disclosure that that WARP interacts with perlecan, and provides Arikawa-Hirasawa (I) or Arikawa-Hirasawa (II) to show the importance of perlecan in skeletal development and component of the cartilage pericellular environment. However, Applicants cannot add to their original assertion to support the enablement issue.

Applicant argues that one skill in the art would extrapolate the results from perlecan to WARP and would expect that perturbations in WARP might lead to defects in ECM integrity.

This scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis. Also, Applicant argues limitation that are not claimed nor disclosed in the specification. Obviousness is not the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

6. Claims 4-5, 12 and 43-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 3/31/06.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (derivative or homolog of WARP) to describe the claimed genus, nor does it provide a description of structural features that are common to species (derivative or homolog of WARP). The specification provides no structural description of WARP derivative or homolog which in situ forms part of the extracellular matrix

other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed derivative or homolog looks like. The specification's disclosure is inadequate to describe the claimed genus of WARP derivative or homolog.

Applicant's arguments, filed 10/2/06 and 11/2/06, have been fully considered, but have not been found convincing.

Applicant points to the specification to support derivative, homolog, 95% and 99% similarity.

However, there is no described or art-recognized correlation or relationship between the structure of the invention, the Willebrand domain of the WARP and it's ECM function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of derivative, homolog, 95% or 99% similarity to SEQ ID NO: 5 which retain the features essential to the instant invention.

The broad brush discussion of making and identifying variants in the specification does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the polypeptide WARP of SEQ ID NO: 6 is disclosed. The specification's general discussion of making and identifying for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 2, 2006

Maher Haddad

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